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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,886	07/24/2003	Robert R. Schmidt	UF-155CD3	5539

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,886	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of SEQ ID NO:1 in the reply filed on 29 June 2005 is acknowledged. However, as a parent application issued with claims to use of all of nucleic acids encoding SEQ ID NOS:2, 4, 24 and 26, the restriction is withdrawn.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method for increasing or decreasing nitrogen metabolism in plants by transformation with a gene encoding a full-length NADP-dependent glutamate dehydrogenase (NADP-GDH) from *Chlorella sorokiniana* or *Escherichia coli* and plants thereby produced, does not reasonably provide enablement for method for increasing or decreasing nitrogen metabolism in plants by transformation with a gene encoding any glutamate dehydrogenase or fragments thereof and plants thereby produced. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims..

The claims are broadly drawn to a method for increasing or decreasing nitrogen metabolism in plants by transformation with a gene encoding any glutamate dehydrogenase or fragments thereof and plants thereby produced.

The instant specification, however, only provides guidance for isolation and kinetic analysis of chloroplast NADP-GDH isozymes from *Chlorella sorokiniana* (example 1), amino-terminal sequencing of the α and β *C. sorokiniana* NADP-GDH subunits and isolation of cDNAs that encode those subunits by hybridization of partial cDNAs with an undefined HCR cDNA probe, and isolation of full-length cDNAs by anchored PCR (pg 21-26), expression of α and β GDH subunits (encoded by SEQ ID NO:23 and 25, respectively) in *Escherichia coli* (pg 26-27), general guidance for plant transformation (pg 27-29), transient expression of the α and β subunits in maize protoplasts (pg 29-31), and general methods for altering codon usage (pg 11-14).

The instant specification fails to provide guidance for production of plants with increased or decreased nitrogen metabolism wherein the plants were transformed with a gene encoding NAD-specific glutamate dehydrogenase (NAD-GDH) or for how the enzyme can function if not targeted to an organelle. The specification also fails to teach nucleic acids encoding fragments of α and β GDH subunits or of their N-terminal portions (SEQ ID NOs:5 and 6), wherein the fragments of α and β GDH subunits have α or β GDH activity and wherein the fragments of the N-terminal portions function as chloroplast transit peptides. The specification also fails to teach plants transformed with the NADP-GDH from *C. sorokiniana* or any other plant.

NAD-GDH is a nuclear-encoded enzyme that functions in mitochondria, while NADP-GDH is a nuclear-encoded enzyme that functions in chloroplasts (specification, pg 2, lines 7-20). The role of NAD-GDH in plants appears to be that of ammonium detoxification and that role is different from that of NADP-GDH because loss of NAD-GDH is not complemented by the presence of NADP-GDH (Oliveira et al, 1997, Plant Physiol. Biochem. 35:185-198, paragraph

spanning pg 191-192). Chavez et al (1995, Plant Mol. Biol. 28:173-188) teach that the role of NADP-GDH is in amination (*i.e.*, the reaction: NH_4^+ + NADPH + 2-oxoglutarate → glutamate + $NADP^+$), while that of NAD-GDH is in deamination (*i.e.*, the reaction: glutamate + NAD^+ → NH_4^+ + NADH + 2-oxoglutarate; pg 174, left column, paragraph 2). Additionally, as NADPH is the reductive nucleotide in the chloroplast, it is not clear that NAD-GDH would even work in the chloroplast. Thus, transformation of a plant with a nucleic acid encoding NAD-GDH, especially if that enzyme is targeted to the chloroplast, is unlikely to alter nitrogen metabolism in that plant. Applicant is invited to submit a declaration showing the results of experiments in which plants were transformed with a nucleic acid encoding NAD-GDH.

The specification fails to teach nucleic acids encoding any NADP-GDH from any organism other than *C. sorokiniana* or *E. coli*. The specification also fails to teach nucleic acids encoding fragments of SEQ ID NOs:2, 4, 24 or 26 that function in the claimed method.

Lastly, while the specification touts the advantages of a plant with increased nitrogen metabolism (*e.g.*, pg 10, lines 4-7, and pg 15, lines 16-17), it fails to describe a use for plants that have decreased nitrogen metabolism. Thus, one would not know how to use such plants.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

4. Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a genus of constructs comprising nucleic acids encoding GDHs. A full review of the specification indicates that nucleic acids encoding GDHs are essential to the operation of the claimed invention. The specification only describes nucleic acids encoding any NADP-GDH from *C. sorokiniana* and *E. coli*, SEQ ID NOs:1, 3, 23 and 25. The specification does not describe fragments of nucleic acids encoding SEQ ID NO:s2, 4, 24 or 26 that encode functional GDHs. Applicant does not describe other nucleic acids encompassed by the claims, and the structural and functional features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described nucleic acids that encode a GDHs within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 22 is indefinite for claim "cells". If one had only one such cell, would it be covered under any issued patent? It is suggested that "Transgenic plant cells" be replaced with --A transgenic plant cell--.

Claims 23-29 recite the limitation "transgenic cells according to claim 22" in line 1. There is insufficient antecedent basis for this limitation in the claims, as claim 2 is drawn to transgenic plant cells.

In claim 26, it is unclear where the chloroplast transit peptide is located in the cell. It is also unclear in what manner the chloroplast transit peptide is adapted when it already targets chloroplasts.

Claim 29 recites the limitation "said tissue specific initiation region" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-5 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Long et al (1994, Plant Physiol. 105:115).

Long et al teach a method of increasing nitrogen metabolism in plant cells by transformation with a construct encoding a bacterial glutamate dehydrogenase, which would

inherently increase the assimilation of inorganic nitrogen (in the form of ammonium) into organic nitrogen. The GDH is operably linked to a chloroplast transit peptide and the construct comprises a polyadenylation sequence. The coding sequence has been altered to use plant-favored codons. The transformed cells would have increased biomass or carbon/nitrogen levels.

9. Claims 1-5, 10, 13-22, 24 and 26-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Lightfoot et al (US Patent 5,998,700, filed July 1996).

Lightfoot et al teach a method for improving the yield of a crop comprising plant a crop that has been transformed with an expressible transgene encoding a bacterial NADP-GDH, and plant cells and plants, including dicots, monocots and Zea mays, transformed with an expression cassette comprising a transcription initiation region, a nucleic acid encoding bacterial NADP-GDH and a transcription termination region, and optionally, a chloroplast transit peptide (claims 1-22). The method would also inherently be one of increasing biomass, increasing total protein, increasing total C/N levels, increasing grain density, and increasing nitrogen metabolism in plants. Lightfoot et al also teach use the constitutive 35S promoter and the seed-specific ubiquitin promoter (Fig 4 and 9; column 7, line 66, to column 26, line 47).

10. Claims 1-5, 10 and 13-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Lightfoot et al (US Patent 6,329,573, filed July 1996).

Lightfoot et al a method comprising growing plants transformed with a nucleic acid encoding bacterial NADP-GDH, and plant cells and plants, including dicots, monocots and Zea mays, transformed with an expression cassette comprising a transcription initiation region, a nucleic acid encoding bacterial NADP-GDH and a transcription termination region, and

optionally, a chloroplast transit peptide; the transcription termination and initiation regions include those not natively associated with the nucleic acid, the transcription initiation regions include those that are constitutive and those that are organ specific, and the nucleic acid is modified to enhance expression in plant cells (claims 1, 4-32). The method would also inherently be one of increasing biomass, increasing total protein, increasing total C/N levels, increasing grain density, increasing the yield and increasing nitrogen metabolism in plants. Lightfoot et al also teach use the constitutive 35S promoter and the seed-specific ubiquition promoter (Fig 4 and 9; column 7, line 66, to column 26, line 47).

11. Claims 1-4, 10, 13 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Good et al (US Patent 6,084,153, filed February 1996).

Good et al teach a method for producing plants and plants cells comprising transforming a plant cell with construct comprising an inducible promoter operably linked to a nucleic acid encoding glutamine dehydrogenase, and optionally regenerating a plant (claims 10-11). Nitrogen metabolism would be inherently increased. The method would also inherently be one of increasing biomass, increasing total protein, increasing total C/N levels, increasing grain density, and increasing plant yield in plants.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-5, 8-10 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Long et al (1994, Plant Physiol. 105:115).

The claims are drawn to a method of increasing or decreasing nitrogen metabolism in a plant by transformation of a gene encoding GDH.

Long et al disclose a method of increasing or decreasing nitrogen metabolism in plant cells by transformation of a gene encoding GDH, as discussed above. Long et al do not disclose regeneration of those cells into whole plants.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of increasing or decreasing nitrogen metabolism in plant cells by transformation of a gene encoding GDH as taught by Long et al, to regenerate those cells into plants. One of ordinary skill in the art would have been motivated to do so to evaluate the performance of the plants in the field.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-4, 7-8, 10-14, 22 and 24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9 of U.S. Patent No. 5,879,941. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method for increasing nitrogen assimilation in plants and plant cells, as claimed in the issued patent, has the same steps as the methods for increasing or decreasing nitrogen metabolism in plant cells, and increasing biomass, increasing total protein, increasing total C/N levels, increasing grain density, and increasing plant yield in plants, as claimed in the instant application; *i.e.*, both comprise the steps of transforming a plant cell with a nucleic acid encoding a protein with glutamate dehydrogenase activity and culturing the cells to produce descendent cells expressing the nucleic acid. The method of the issued patent could also be considered a species of the genus of the methods of increasing or deceasing nitrogen metabolism is n a plant, as claimed in the instant application, as evidenced by dependent claim 3 in the instant application. Furthermore, the method of the issued patent is drawn to use of nucleic acids encoding SEQ ID NOs:2, 4, 24 and 26, as is the method of the instant application. Dependent claims in both are drawn to the nucleic acid being operably linked to a plant polyadenylation sequence and to use of a plant expressible promoter.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (571) 272-0745.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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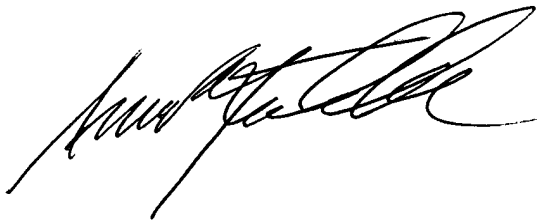
Anne R. Kubelik, Ph.D.
September 2, 2005



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